## (FILE 'HOME' ENTERED AT 16:56:52 ON 27 MAR 2009)

FILE 'MEDLINE, CAPLUS, SCISEARCH' ENTERED AT 17:09:17 ON 27 MAR 2009 L1 91912 S MYELOMA

L2 390 S L1 AND TRANSFERRIN

L3 392 S L1 AND (IRON OR FERRIC OR FERROUS)

L4 304 DUP REM L3 (88 DUPLICATES REMOVED)

L5 19 S L4 AND MEDIA

L6 19 DUP REM L5 (0 DUPLICATES REMOVED)

L7 12 S L6 AND PY<=2003

L8 1 S L7 AND CHELATOR

L9 1 S L8 AND TRANSFERRIN

L10 7 S L7 AND TRANSFERRIN

L11 1 S L7 AND TRANSFERRIN AND TROPOLONE

## => d ti 1-12, 17

- L7 ANSWER 1 OF 12 MEDLINE on STN
- TI Improved fermentation processes for NSO cell lines expressing human antibodies and glutamine synthetase.
- L7 ANSWER 2 OF 12 MEDLINE on STN
- TI [Analysis of causes for anemia in patients with multiple myeloma].
  Analiza przyczyn niedokrwistosci u chorych na szpiczaka mnogiego.
- L7 ANSWER 3 OF 12 MEDLINE on STN
- TI The protein hydrolysate, Primatone RL, is a cost-effective multiple growth promoter of mammalian cell culture in serum-containing and serum-free media and displays anti-apoptosis properties.
- L7 ANSWER 4 OF 12 MEDLINE on STN
- TI [The cultivation of mouse and human lymphoid cells on serum-free media].

Kul'tivirovanie limfoidnykh kletok myshi i cheloveka v bessyvorotochnykh sredakh.

- L7 ANSWER 5 OF 12 MEDLINE on STN
- TI Optimisation of hybridoma cell growth and monoclonal antibody secretion in a chemically defined, serum— and protein—free culture medium.
- L7 ANSWER 6 OF 12 MEDLINE on STN
- TI Studies on the uptake of 67 Ga and 59 Fe and the binding of transferrin by cultured mouse tumour cells.
- L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
- TI Iron-containing nanoparticles with double coating and their use in diagnosis and therapy
- L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
- TI Improved culture method using citrate for mammalian cell in vitro proliferation
- L7 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
- TI Chemically defined medium for cultured mammalian cells
- L7 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
- II Serum-free animal tissue culture medium for mass production of proteins
- L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
- TI Iron chelate culture medium additive

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN TI Synthetic culture media for hybridomas and myelomas

=> d ibib abs 1, , 5, 8, 9, 10, 11, 12

1 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE The answer numbers requested are not in the answer set. ENTER ANSWER NUMBER OR RANGE (1):1

L11 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 2003063223 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12573022

TITLE: Improved fermentation processes for NSO cell lines expressing human antibodies and glutamine synthetase.

AUTHOR: Dempsey Jonathan; Ruddock Steve; Osborne Matthew; Ridley

Alison; Sturt Simone; Field Ray

CORPORATE SOURCE: Cambridge Antibody Technology, The Science Park, Melbourn,

Cambridgeshire SG8 6JJ, United Kingdom.

SOURCE: Biotechnology progress, (2003 Jan-Feb) Vol. 19,

No. 1, pp. 175-8.

Journal code: 8506292. ISSN: 8756-7938.

PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)

(EVALUATION STUDIES)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200310

ENTRY DATE: Entered STN: 8 Feb 2003 Last Updated on STN: 8 Oct 2003

Entered Medline: 7 Oct 2003

To meet the increasing requirement for therapeutic antibodies to conduct AB clinical trials, an enhanced culture medium and fed-batch process was developed for GS-NSO cell lines. This process was shown to produce high concentrations of monoclonal antibodies for several cell lines expressing different antibodies. Cells were adapted to growth in a glutamine- and serum-free medium containing bovine serum albumin (BSA), cholesterol, and transferrin. A number of amino acids were found to be depleted during cell culture. The concentrations of these amino acids were increased, and further cell culture analyses were performed. This process of cell growth and analysis was repeated over multiple cycles until no depletion was detected. This resulted in an amino acid supplement that was shown to be generic and enhanced antibody productivity up to 5-fold for the three cell lines tested. Transferrin was replaced using tropolone, a lipophilic iron chelator and ferric ammonium citrate. Cell growth was equivalent to that in transferrin-containing medium over the wide ranges tested. A concentrated feed solution, based on the amino acid supplement and the components of the serum- and protein-free supplements, was formulated. Addition of this feed in response to metabolic requirements resulted in a harvest titer a further 2-fold higher than the enhanced culture medium. Harvest antibody titers of up to 600 mg/L were achieved for three cell lines expressing different antibodies, representing an increase of 10-fold over the starting concentrations.

<sup>=&</sup>gt; d ibib abs 1, 5, 8, 9, 10, 11, 12 17

DOCUMENT NUMBER: PubMed ID: 12573022

TITLE: Improved fermentation processes for NSO cell lines
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AUTHOR: Demosev Jonathan; Ruddock Steve; Osborne Matthew; Ridley

Alison; Sturt Simone; Field Ray

CORPORATE SOURCE: Cambridge Antibody Technology, The Science Park, Melbourn,

Cambridgeshire SG8 6JJ, United Kingdom.

SOURCE: Biotechnology progress, (2003 Jan-Feb) Vol. 19,

No. 1, pp. 175-8.

Journal code: 8506292, ISSN: 8756-7938.

PUB. COUNTRY: United States

DOCUMENT TYPE: (COMPARATIVE STUDY)

(EVALUATION STUDIES)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: ENTRY DATE:

Entered STN: 8 Feb 2003

Last Updated on STN: 8 Oct 2003 Entered Medline: 7 Oct 2003

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different antibodies. Cells were adapted to growth in a glutamine- and serum-free medium containing bovine serum albumin (BSA), cholesterol, and transferrin. A number of amino acids were found to be depleted during cell culture. The concentrations of these amino acids were increased, and further cell culture analyses were performed. This process of cell growth and analysis was repeated over multiple cycles until no depletion was detected. This resulted in an amino acid supplement that was shown to be

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L7 ANSWER 5 OF 12 MEDLINE on STN

ACCESSION NUMBER: 1989124403 MEDLINE DOCUMENT NUMBER: PubMed ID: 2644356

TITLE: Optimisation of hybridoma cell growth and monoclonal antibody secretion in a chemically defined, serum— and

protein-free culture medium.

AUTHOR: Schneider Y J

CORPORATE SOURCE: Universite Catholique de Louvain, Departement de Biochimie

et de Biologie Cellulaire, Brussels, Belgium. Journal of immunological methods, (1989 Jan 6)

Vol. 116, No. 1, pp. 65-77.

Journal code: 1305440. ISSN: 0022-1759.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198903

SOURCE:

ENTRY DATE: Entered STN: 8 Mar 1990

## Last Updated on STN: 6 Feb 1998 Entered Medline: 21 Mar 1989

AB Monoclonal antibodies (MAbs), for human use require chemical and biological purity. The best approach seems in vitro cultivation in a serum-, protein-free medium. A basal defined culture medium has been developed to sustain optimal hybridoma cell growth and MAb secretion. It consists of Iscove's Dulbecco's modified, Eagle's, Ham's F12 and NCTC 135 media in a 5:5:1 mixture (v/v/v), to which glucose is added to reach a final concentration of 25 mM, glutamine to 4-6 mM, 2-mercaptoethanol to 50 microM, Pluronic F68 to 0.01-0.1% (w/v), Hepes to 25 mM and NaHCO3 to 3 g/l. Hybridoma cells, derived from Sp 2/0 myeloma and secreting a MAb to a human milk fat globule membrane-associated high molecular weight glycoprotein, were cloned in this medium containing 1% (v/v) fetal calf serum and then sequentially adapted in serum-free medium further supplemented with transferrin and insulin, both at 10 micrograms/ml. Clones producing immunoreactive MAbs secrete a mean of 50 micrograms IgG/ml, i.e., ca. 80% of the concentration reached in Dulbecco's modified Eagle's medium containing 10% serum. When cells were cultured in spinner flasks with a semi-continuous mode of cultivation (with a daily removal of 20% of the volume and its replacement by fresh culture medium), in serum-free medium further supplemented with 10 nM estradiol, a mixture of trace elements and albumin (at 30 micrograms/ml) complexed to linoleic acid, MAb secretion reached 100 micrograms/ml and became equal or higher to that obtained in serum-containing medium. MAb secretion was not decreased and was even significantly increased during the growth phase, when transferrin was replaced by another iron source, i.e., ferric citrate at 500 microM associated with 20 microM ascorbic acid. Finally, deletion of insulin and of albumin-linoleic acid did not affect significantly cell density nor MAb secretion. In conclusion, it appears from this study that semi-continuous cultivation in spinner flasks of hybridoma cells, after cloning and progressive adaptation, in a chemically defined, serum- and protein-free medium, permitted MAb secretion to be increased to a mean of 144 micrograms/ml, i.e., multiplied by a factor of ca. 1.5 compared to culture of these cells in serum-containing medium under the same conditions and by a factor of ca. 2.4 compared to cultivation in serum-containing medium in flasks.

L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:702847 CAPLUS

DOCUMENT NUMBER: 139:226837

TITLE: Improved culture method using citrate for mammalian

cell in vitro proliferation

INVENTOR(S): Urlich, Balent; Horst, Everhad; Bartort, Schutzperky

PATENT ASSIGNEE(S): F. Hoffmann-La Roche & Co. AG, Switz.
SOURCE: Jpn. Kokai Tokkvo Koho, 6 pp.

CODEN: JKXXAF

Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

DOCUMENT TYPE:

	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP	2003250533	A	20030909	JP 2003-58803	20030305 <
CA	2417689	A1	20030905	CA 2003-2417689	20030130 <
CA	2417689	C	20060509		
MX	2003001487	A	20050908	MX 2003-1487	20030218
IN	2003MA00155	A	20071221	IN 2003-MA155	20030227
US	20030175951	A1	20030918	US 2003-376392	20030303 <
US	7390660	B2	20080624		

EP 1342780 A1 20030910 EP 2003-4806 20030304 <-- EP 1342780 B1 20050907 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK AT 304047 T 20050915 AT 2003-4806 20030304 ES 2248657 Т3 20060316 ES 2003-4806 20030304 CN 1442478 20030917 CN 2003-107060 20030305 <--A CN 100398640 С 20080702 EP 2002-4366 PRIORITY APPLN. INFO.: A 20020305 AB An improved culture method for mammalian cell in vitro proliferation is provided, with which the glucose consumption and/or lactate formation upon mammalian cell proliferation are simply reduced. The method is characterized in that the cell culture is performed in the presence of a bicarbonic acid or tricarbonic acid or its salt (e.g., citric acid, citrate) of ca. 1-50mmol/1. For example, free citric acid or citrate (e.g., alkali metal salt) of this quantity was added to the culture medium rather than citric acid in the form of a chelate complex with iron or other transition metal ion.

L7 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

2002:658225 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 137:184584

TITLE: Chemically defined medium for cultured mammalian cells INVENTOR(S): Lee, Chichang: Lv. Celia: Moore, Gordon: Perkinson,

Robert. PATENT ASSIGNEE(S):

Centocor, Inc., USA SOURCE: PCT Int. Appl., 29 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO.				KIN		DATE						NO.			ATE			
WO	WO 2002066603 WO 2002066603			A2								74			0020	205	<	
		AE, CO, GM, LS, RO,	AG, CR, HR, LT, RU,	AL, CU, HU, LU,	AM, CZ, ID, LV, SE,	AT, DE, IL, MA,	AU, DK, IN, MD,	AZ, DM, IS, MG, SK,	BA, DZ, JP, MK,	EC, KE, MN,	EE, KG, MW,	ES, KP, MX,	FI, KR, MZ,	GB, KZ, NO,	GD, LC, NZ,	GE, LK, PL,	GH, LR, PT,	
	RW:	CY,	DE,	DK,	ES,	FI,	FR,	SD, GB, GA,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	
CA	2438	148			A1		2002	0829		CA 2	002-	2438	148		2	0020	205	<
AU	2002	2438	24		A1		2002	0904		AU 2	002-	2438	24		2	0020	205	<
US	2003	0096	402		A1		2003	0522		US 2	002-	6738	2		2	0020	205	<
	6900							0531										
EP	1360									EP 2	002-	7093	35		2	0020	205	<
EP	1360	314			B1		2009	0114										
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR							
JP	2005	5052	40		T		2005	0224		JP 2	002-	5663	10		2	0020	205	
AT	4209	45			T		2009	0115		AT 2	002-	7093	35		2	0020	205	
	2008															0800	325	
PRIORIT	Y APP	LN.	INFO	. :						US 2	001-	2688	49P		P 2	0010	215	
										JP 2	002-	5663	10		A3 2	0020	205	
										WO 2	002-	US32	74		W 2	0020	205	

media for growth of mammalian cells for production of com. useful

amts. of expressed proteins.

REFERENCE COUNT: THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1996:290368 CAPLUS DOCUMENT NUMBER: 124:341059

ORIGINAL REFERENCE NO.: 124:63353a,63356a TITLE: Serum-free animal tissue culture medium for mass

production of proteins INVENTOR(S): Sawada, Hidekazu; Ito, Takashi; Maejima, Kazutaka

PATENT ASSIGNEE(S): Takeda Chemical Industries Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF DOCUMENT TYPE: Patent LANGUAGE . Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
JP 08070859	A	19960319	JP 1995-150683		19950616	<
PRIORITY APPLN. INFO.:			JP 1995-150683	A	19950616	
			JP 1994-144172		19940627	

A serum-free animal tissue culture medium composition containing inorg. or organic Fe

compds., cyclodextrin, non-ionic surfactants, and, optionally, insulin, ethanolamine, and selenites is provided. The medium may supplemented with dexamethasone, protein hydrolyzates, and amino acids. Production of t-gD-IL-2, a fusion protein of herpes simplex virus (HSV) type 1 glycoprotein D (t-gD) and human interleukin-2 (IL-2), by cultivating mouse

myeloma cell strain Sp2/0-22-32-34 in this medium was demonstrated.

L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:512962 CAPLUS

DOCUMENT NUMBER: 119:112962 ORIGINAL REFERENCE NO.: 119:20212h, 20213a

TITLE: Iron chelate culture medium additive

INVENTOR(S): Suhr-Jessen, Peter Bernt PATENT ASSIGNEE(S): Novo Nordisk A/S, Den. SOURCE: PCT Int. Appl., 15 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE	
WO 9300423		A1	19930107	WO 1992-DK190	19920618	<
W: AU,	CA, JP,	US				
RW: AT,	BE, CH,	DE, DK	, ES, FR,	GB, GR, IT, LU, MC,	NL, SE	
CA 2111984		A1	19930107	CA 1992-2111984	19920618	<
AU 9221968		A	19930125	AU 1992-21968	19920618	<
EP 593539		A1	19940427	EP 1992-913614	19920618	<
R: AT,	BE, CH,	DE, DK	, ES, FR,	GB, GR, IT, LI, LU,	NL, SE	
JP 06508523		T	19940929	JP 1992-501299	19920618	<
PRIORITY APPLN.	INFO.:			EP 1991-610054	A 19910621	
				NO 1002 DE100	7 10020610	

AB A culture medium additive comprises a chelate of a soluble Fe salt and an alkali metal or alkaline earth metal citrate. The additive is a suitable Fe source for serum-free or protein-free culture media. BHK cells, CHO cells, SP2/0 myeloma cells, and SP2/0-based hybridoma cells were cultivated in serum-free nutrient media supplemented with Na citrate-Fe chloride chelate.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1989:455870 CAPLUS DOCUMENT NUMBER: 111:55870 ORIGINAL REFERENCE NO.: 111:9493a,9496a

TITLE: Synthetic culture media for hybridomas and

myelomas

INVENTOR(S): Kovar, Jan; Franek, Frantisek

PATENT ASSIGNEE(S): Ceskoslovenska Akademie Ved, Czech.

Fr. Demande, 9 pp. SOURCE:

CODEN: FRXXBL DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE			
	FR 2604727	A1	19880408	FR 1987-13651		19871002	<		
	FR 2604727	B1	19900518						
	GB 2196348	В	19900704	GB 1987-22473		19870924	<		
	PRIORITY APPLN. INFO.:			CS 1986-7158		19861003			
	AB Synthetic media fo	r cultur	ing of hybr	cidomas and myelomas					
	contain iron salts. An RPMI medium containing, in addition to salts,								
	ethanolamine, ascorbic acid, and hydrocortisone, ferric citrate								
5 + 10-4M was prepared and hybridoma PLV-01 was cultured in it.									
	Growth in this medium was comparable to growth in medium SFH (without								
	linoleic acid and	albumin)	of Kovar a	and Franek (Meth. En	zymol	. (1986)			
	121:277).				_				

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT